## (19) World Intellectual Property Organization

International Bureau



534582

# 

(43) International Publication Date 10 June 2004 (10.06.2004)

PCT

### (10) International Publication Number WO 2004/048374 A1

- (51) International Patent Classification<sup>7</sup>: C07D 471/04. A61K 31/4375, A61P 25/00, C07D 471/04, 221/00, 221/00
- (21) International Application Number:

PCT/CA2003/001800

(22) International Filing Date:

19 November 2003 (19.11.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/428,611

22 November 2002 (22.11.2002)

- (71) Applicant (for all designated States except US): MERCK FROSST CANADA & CO. [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): DUBE, Daniel [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA). GALLANT, Michel [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA). LACOMBE, Patrick [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA). ASPIOTIS, Renee [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA). DUBE, Laurence [CA/CA]; 16711 Trans-Canada Highway, Kirkland,

Québec H9H 3L1 (CA). GIRARD, Yves [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA). MACDONALD, Dwight [CA/CA]; 16711 Trans-Canada Highway, Kirkland, Québec H9H 3L1 (CA).

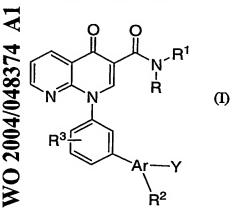
- (74) Agents: OGILVY RENAULT et al.; Suite 1600, 1981 McGill College Avenue, Montreal, Québec H3A 2Y3 (CA).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: 4-OXO-1-(3-SUBSTITUTED PHENYL-1,4-DIHYDRO-1,8-NAPHTHYRIDINE-3-CARBOXAMIDE PHOSPHODI-**ESTERASE-4 INHIBITORS** 



(57) Abstract: Compounds represented by Formula (I):or a pharmaceutically acceptable salt thereof, are phosphodiesterase 4 inhibitors useful in the treatment of asthma and inflammation and useful for the enhancement of cognition.

#### INTERNATIONAL SEARCH REPORT

ational Application No A 03/01800

CLASSIFICATION OF SUBJECT MAPC 7 CO7D471/04 A61K31/4375 A61P25/00 //(C07D471/04,221:00, 221:00) According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 CO7D A61K A61P Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the International search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Category ° Relevant to claim No. Α WO 99 07704 A (SUNTORY) 1,25,32 18 February 1999 (1999-02-18) page 2, line 32 -page 3, line 12; claim 1 P,X WO 02 094823 A (MERCK FROSST CANADA) 1,22-26,28 November 2002 (2002-11-28) claims 1,21-24,27; examples 24,61 Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled document referring to an oral disclosure, use, exhibition or other means document published prior to the International filing date but later than the priority date claimed in the art. "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report

25/02/2004

Alfaro Faus, I

Authorized officer

Name and mailing address of the ISA

17 February 2004

Fax: (+31-70) 340-3016

European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,





Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	mational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Although claims 25-28 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds.
2.	Claims Nos.: because they relate to parts of the international Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carried out, specifically:
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	rnational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
. —	
3.	As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark	on Protest The additional search fees were accompanied by the applicant's protest.
	No protest accompanied the payment of additional search fees.

#### INTERNATIONAL SEARCH REPORT

Information on patent family members

In CA 03/01800

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9907704	A	18-02-1999	AU	755350 B2	12-12-2002
			ΑU	8560798 A	01-03-1999
			CA	2268190 A1	18-02-1999
			CN	1239478 T	22-12-1999
			EP	0958297 A1	24-11-1999
			HU	0001054 A2	28-10-2000
			WO	9907704 A1	18-02-1999
			JP	11106385 A	20-04-1999
			US	6297248 B1	02-10-2001
			US	2002006935 A1	17-01-2002
WO 02094823	A	28 <b>-</b> 11-2002	WO	02094823 A1	28-11-2002
			US	2003096829 A1	22-05-2003